REMARKS

Claims 1-36 are pending. Claims 1-9 and 24-26 are currently under examination. Claim 1 is canceled herein, and replaced with new claim 37. Claim 2 is canceled herein. Claims 10-23 and 27-36 are withdrawn from consideration. Claims 3, 4, 8, 9, 24 and 25 are amended herein. The amendments to claims 3, 4, 8, 9 and 25 are made to change the dependency from canceled claim 1 to new claim 37. The amendments add no new matter.

Claim Objection:

Claim 1 is objected to for a grammatically incorrect comma in the first line. Applicants submit that the cancellation of claim 1 herein renders this objection moot.

Rejection under 35 U.S.C. §112, Second Paragraph:

Claim 24 is rejected as indefinite under §112, second paragraph. The Office Action states:

> It would appear that Applicant intends that the claim read on a pair of polypeptides, wherein a first polypeptide of the pair is labeled with a fluorescent dye and a second polypeptide of the pair is a recombinant fusion polypeptide according to claim 1. However, the claim, as written, can also be understood to read on a pair of polypeptides wherein both polypeptides are labeled with a fluorescent dye and a recombinant fusion polypeptide of claim 1. It is suggested that Applicant amend the claim to clearly set forth the limitations of each polypeptide of the pair.

Applicants submit that claim 24 as amended is definite. Specifically, Applicants have amended claim 24 to refer separately to the two members of the pair, as in "A pair of polypeptides, *one member of said pair* comprising...., *and the other member of said pair comprising*...." The amendment adds no new matter. Applicants respectfully request the withdrawal of this §112, second paragraph rejection.

Rejections under 35 U.S.C. §102:

Claims 1 and 4-9 are rejected under 35 U.S.C. §102(b) as anticipated by von Arnim et al., 1998, Gene 221: 35-43. The Office Action states:

> von Arnim et al. teaches a recombinant tandem dimer of GFP and GFP fused to COP9 and FUS6. It is understood in the art, and acknowledged in the

> specification that GFP is found in nature as a monomer of a multimeric protein. vonArnim et al. teaches that COP9 and FUS6 are part of a nuclear protein complex and are therefore also found in nature as monomers of a multimeric protein. As the recombinant fusion polypeptides of von Arnim et al. each comprise at least one GFP moiety, the fusion polypeptide is fluorescent when excited. Further, none of the fusion polypeptides form a fluorescent donor-acceptor pair.

The Office Action continues:

> In addition, Arnim et al. teaches fusion of a third GFP molecule to the GFP tandem dimer to form a fusion polypeptide further comprising a third polypeptide peptide bonded to the recombinant fusion polypeptide, wherein the third polypeptide is a member of a specific binding pair according to the limitations of claims 4 and 5.

The Office Action concludes that the claims are anticipated by the von Arnim et al. reference. Applicants respectfully disagree.

Applicants submit that the cancellation of claim 1 herein renders this rejection moot as to that claim. Applicants submit that new claim 37, which replaces claim 1, is novel over von Arnim et al. The language of the amended claim is supported throughout the specification, but specifically at page 21, lines 17-19, page 15, lines 1-15, and page 26, lines 10-20, each referring to linker sequences.

Applicants submit that von Arnim et al. does not teach a recombinant fusion in which the first polypeptide is peptide bonded to the second polypeptide via a linker sequence as required by claim 37. The von Armin at al. reference refers to "a head-to-tail dimer of GFP (55 kDa)" and "a trimer of GFP (83 kDa)" but does not teach a linker sequence between the members of the dimer or, for that matter the trimer. Because von Arnim et al. does not teach a linker sequence, the reference does not anticipate claim 37 or those claims that depend from it.

Claims 1-3 and 24 are rejected under 35 U.S.C. 102(b) as being anticipated by Wouters et al. (September 1999) *Curr. Biol.* 9:1127-1130. The Office Action states that Wouters et al. teaches "a recombinant fusion polypeptide comprising an EGF receptor fused to GFP, wherein the EGF receptor is found in nature as a monomer of a multimeric protein (i.e., EGF receptor dimer; see Figure 1) and GFP is also a monomer of a multimeric protein." The Office Action further states that "the EGF receptor and GFP are not fluorescent donor and acceptor to each

other and the fusion polypeptide is fluorescent when excited (see especially Figure 2 and the caption thereto). The Office Action thus concludes that the teachings of Wouters et al. meet the limitations of claims 1-3. With respect to claim 24, The Office Action states that Wouters et al. "also teaches a pair of polypeptides comprising a first polypeptide labeled with a fluorescent dye (i.e., Cy3-anti-PY) and the second polypeptide which is the EGF receptor-GFP fusion protein described above, wherein the fluorescent dye and recombinant fusion polypeptide are fluorescent donor and acceptor to each other (see especially Figure 1 and the caption thereto)." The Office Action thus concludes that Wouters et al. anticipates claim 24. Applicants respectfully disagree.

As noted above, the rejection is moot as applied to claim 1. The same is true of claim 2, which is canceled herein. Applicants submit that Wouters et al. does not teach the invention of replacement claim 37 because the reference does not teach that "said first and said second polypeptides are monomers of a multimeric fluorescent protein." Specifically, EGF is not a monomer of a multimeric fluorescent protein.

Applicants submit that the Wouters et al. reference does not satisfy the limitations of claim 24 because claim 24 as amended is now dependent from new claim 37, which is not anticipated by Wouters et al. for the reason discussed above.

Claims 1-3 and 25 are rejected under 35 U.S.C. 102(b) as being anticipated by Periasamy *et al.* (1997) In Functional Imaging and Optical Manipulation of Living Cells, Proc. SPIE 2983, ed. DL Farkas, BJ Tromberg. Belingham, WA: SPIE. The Office Action states:

> Periasamy *et al.* teaches recombinant fusion polypeptides comprising Pit-1 fused to GFP and BFP, wherein Pit-1 is found in nature as a monomer of a multimeric protein (i.e., Pit-1 homodimer; third paragraph on page 64) and GFP is also a monomer of a multimeric protein (*Id.*). Pit-1 and GFP or BFP are not fluorescent donor and acceptor to each other and the fusion polypeptide is fluorescent when excited (see especially the first full paragraph on page 62 and Figure 2). Thus, the fusion proteins of Periasamy *et al.* meet all of the limitations of the recombinant fusion polypeptide of claim 1. Further, Periasamy *et al.* teaches that the GFP-Pit-1 fusion protein comprises a 5 amino acid linker according to the limitations of claims 2 and 3 (see especially lines 8-9 on page 60); and, as the GFP and BFP fusion proteins of Periasamy *et al.* are fluorescent donor and acceptor to each other, the fusion protein pair of Periasamy *et al.* also meets the limitations of claim 25.

Applicants respectfully disagree.

As with the previous rejection, this rejection is moot with regard to claims 1 and 2. Applicants submit that Periasmy et al. does not anticipate replacement claim 37 because the reference does not teach that "said first and said second polypeptides are monomers of a multimeric fluorescent protein" as required by the claim. Specifically, Pit-1 is not a monomer of a multimeric fluorescent protein. As such, the reference fails to satisfy all elements of the claim and cannot anticipate the claim or dependent claims 3 and 25 which are now dependent from claim 37 instead of canceled claim 1.

Claim 1 is rejected under 35 U.S.C. 102(b) as being anticipated by Oker-Blom et al. (1996) FEBS Lett. 389:238-243 as evidenced by the NiceProt view of Swiss-Prot: P22629 (available at http://us.expasy.org/). The Office Action states:

> Oker-Blom et al. teaches recombinant fusion polypeptide comprising streptavidin fused to GFP, wherein streptavidin is found in nature as a monomer of a multimeric protein (i.e., streptavidin homotetramer; see NiceProt view of Swiss-Prot: P22629) and GFP is also a monomer of a multimeric protein (Id.). Streptavidin and GFP are not fluorescent donor and acceptor to each other and the fusion polypeptide is fluorescent when excited (see especially Figure 2 and the caption thereto). Thus, the fusion protein of Oker-Blom *et al.* anticipates all of the limitations of the recombinant fusion polypeptide of claim 1.

Applicants respectfully disagree.

As with the previous rejection, this rejection is moot with regard to claim 1. Applicants submit that Oker-Blom et al. does not anticipate replacement claim 37 because the reference does not teach that "said first and said second polypeptides are monomers of a multimeric fluorescent protein" as required by the claim. Specifically, Streptavidin is not a monomer of a multimeric fluorescent protein. As such, the reference fails to satisfy all elements of the claim and cannot anticipate it.

In view of the above, Applicants submit that new claim 37 and the claims dependent from it are novel over the references cited. Applicants respectfully request the withdrawal of the §102 rejections of these claims.

Allowable Subject Matter:

Applicants appreciate the Examiner's acknowledgment that claim 26 would be allowable if re-written in independent form including all of the limitations of the base claim and any

intervening claims. Applicants have not amended claim 26 at this time because new claim 37, from which it ultimately depends, is believed to be allowable.

In view of the above, Applicants submit that all issues raised in the Office Action have been addressed. Reconsideration of the claims is respectfully requested.

Respectfully submitted,

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